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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
253625

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

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Application Number	Filed
10/586,072	July 14, 2006

First Named Inventor
Brough

Art Unit	Examiner
1632	Wu Cheng Winston Shen

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 51,860.
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

/Melissa E. Kolom/
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September 14, 2010
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

REASONS FOR PRE-APPEAL BRIEF REQUEST FOR REVIEW

Status of Claims

Claims 35, 39-42, 45-48, 52, and 53 are pending and are the subject of this appeal.

Summary of Claimed Subject Matter

The appealed claims are directed to a method of changing the sensory perception of an animal. The method comprises administering to the inner ear a pharmaceutical composition comprising a serotype 28 adenoviral vector (Ad28), wherein the Ad28 adenoviral vector comprises a nucleic acid sequence encoding Hath1 operably linked to a promoter that functions in supporting cells of the inner ear. The nucleic acid sequence is expressed to produce Hath1, thereby resulting in generation of sensory hair cells that allow perception of stimuli in the inner ear (see the specification at, for example, paragraphs 0007, 0009, 0010, 0024, 0044, 0055, and 0063).

Grounds of Rejection to be Reviewed

Claims 35, 39, and 40 are rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of the combination of U.S. Patent 6,838,444 (Zoghbi et al.), U.S. Patent 5,837,511 (Falck-Pedersen et al.), U.S. Patent 6,913,922 (Bout et al.), and Wigand et al. (*Arch. Virol.*, *64*(3): 225-233 (1980)).

Claims 41 and 42 are rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of the combination of Zoghbi et al., Falck Pedersen et al., Bout et al., Wigand et al., and U.S. Patent 6,821,775 (Kovesdi et al.).

Claims 45-48 are rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of the combination of Zoghbi et al., Falck Pedersen et al., Bout et al., Wigand et al., and Staecker et al. (*Otolaryngol. Head Neck Surg.*, *119*(1): 7-13 (1998)).

Claims 52 and 53 are rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of the combination of Zoghbi et al., Falck Pedersen et al., Bout et al., Wigand et al., U.S. Patent 6,455,314 (Wickham et al.), and Mizuguchi et al. (*Gene Ther.*, *9*(12):769-776 (2002)).

Reasons for Withdrawal of Rejection

The Office has failed to establish a *prima facie* case of obviousness because (1) the Office has not provided a credible reason for one of ordinary skill in the art to have combined, and then follow, the teachings of the cited references, and (2) the Office has not accorded appropriate weight to the Rule 132 declarations of record.

1. The Office Has Not Provided a Credible Reason to Combine the Cited References

Appellants maintain that one of ordinary skill in the art would not have chosen a serotype 28 adenoviral vector (Ad28) for the purposes of delivering a nucleic acid sequence encoding Hath1 operably linked to a promoter that functions in supporting cells of the inner ear, as required by the appealed claims.

As the Supreme Court recently stated, "*there must be some articulated reasoning* with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418, 82 U.S.P.Q.2d 1385, 1396 (2007) (emphasis added)). With respect to the present application, the Office has failed to articulate any reasoning with a rational underpinning to support the obviousness rejection in view of the cited references.

Zoghbi et al. teaches a method of generating hair cells in a mammal using adenoviral vectors to deliver an atonal-associated nucleic acid. Falck-Pedersen et al. discloses methods for generating replication-deficient non-group C adenoviral vectors (i.e., subgroups A, B, D, E, and F).

Bout et al. discloses that different adenovirus serotypes exhibit different tropisms. For example, Bout et al. discloses that adenovirus serotypes 2, 4, 5, and 7 have a natural tropism for lung epithelia and other respiratory tissues, while serotypes 40 and 41 have a natural tropism for the gastrointestinal tract. Bout et al. also discloses replication-deficient adenoviral vectors based on serotype 35 or 11, or chimeric vectors comprising a portion of the Ad35 or Ad11 genome.

Wigand et al. discloses the isolation of a serotype 36 adenovirus (Ad36), which is characterized as belonging to subgroup D. Wigand et al. discloses that Ad36 is distinct both in neutralization and hemagglutination-inhibition from all other human adenoviruses, and

exhibits a unique DNA restriction pattern. Wigand et al. also discloses that the DNA structure of Ad36 is closely related to Ad28 and other subgroup D adenoviruses.

The Office has conceded that each of Zoghbi et al., Falck Pedersen et al., and Bout et al. does not explicitly teach or suggest a method of changing sensory perception in an animal by administering the specifically selected adenoviral vector recited in the pending claims, namely an Ad28 vector comprising Hath1. In view of the disclosure of Wigand et al., however, the Office has concluded that one of ordinary skill in the art would have been motivated to use an adenoviral vector based on serotype 28 based on its similarity to Ad36.

However, one of ordinary skill in the art would not have had a credible reason to choose Ad28 for use in the context of a method such as described by Zoghbi et al. with a reasonable expectation of success based on the disclosure of Falck-Pedersen et al., Bout et al., and/or Wigand et al. In this regard, while Wigand et al. discloses that the genomes of Ad36 and Ad28 are similar, Wigand et al. also states that Ad36 is genetically similar to other subgroup D adenoviruses. There is nothing in the Wigand reference that would have provided a reason for one of ordinary skill in the art to have specifically selected Ad28 from among the more than 20 serotypes within subgroup D, much less from among the 51 adenoviral serotypes known in the art (such as those disclosed in Falck-Pedersen et al. and Bout et al.). Moreover, one of ordinary skill in the art at the time of the present invention would have known that Ad36 disadvantageously infects cells of adipose tissue (see, e.g., Dhurandhar et al., *Int. J. Obes. Relat. Metab. Disord.*, *24*(8): 989-996 (2000), and Dhurandhar et al., *Int. J. Obes. Relat. Metab. Disord.*, *25*(7): 990-996 (2001)). Thus, if anything, one of ordinary skill in the art at the time of the claimed invention would have been led away from using Ad36 and other closely related serotypes, such as Ad28, to transduce cells of the inner ear. Thus, using the Office's reasoning, the art available at the time of the claimed invention *taught away* from using Ad28 to transduce inner ear cells.

In addition, selecting an adenovirus of a specific serotype from a given subgroup is not simply a matter of "routine optimization," as the Office has alleged. The Federal Circuit has held that differences in *concentration or temperature* will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. See *Merck & Co., Inc. v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 10 U.S.P.Q.2d 1843 (Fed. Cir. 1989), *cert. denied*, 493 U.S. 975 (1989), and *In re Geisler*, 116 F.3d 1465, 43 U.S.P.Q.2d 1362 (Fed. Cir. 1997). Similarly, a *prima facie*

case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. See *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 U.S.P.Q. 773 (Fed. Cir. 1985). The selection of a distinct organism (i.e., an adenovirus of a particular serotype) from among a group of related but different organisms (i.e., an adenovirus subgroup) is much different than the routine adjustment of the conditions of a particular chemical reaction or process. While adenoviruses of different serotypes within the same subgroup share structural similarities, such adenoviruses are different enough that one of ordinary skill in the art would not expect adenoviruses within a particular subgroup to have the same properties.

For the foregoing reasons, however, one of ordinary skill in the art would not have had a credible reason to utilize a serotype 28 adenoviral vector to deliver a nucleic acid sequence encoding Hath1 to the inner ear, with a reasonable expectation of success, based on the combined disclosures of Zoghbi et al., Falck Pedersen et al., Bout et al., and Wigand et al.

None of the secondary references compensates for the deficiencies of Zoghbi et al., Falck Pedersen et al., Bout et al., and Wigand et al. In this respect, Kovesdi et al., Staecker et al., Wickham et al., and Mizuguchi et al. do not disclose or suggest a serotype 28 adenoviral vector which comprises a nucleic acid sequence encoding Hath1 operably linked to a promoter that functions in supporting cells of the inner ear, much less a method of using such an adenoviral vector to change the sensory perception of an animal. Therefore, Kovesdi et al., Staecker et al., Wickham et al., and Mizuguchi et al. fail to provide a credible reason for one of ordinary skill in the art to utilize a serotype 28 adenoviral vector to deliver a nucleic acid sequence encoding Hath1 to the inner ear, with a reasonable expectation of success, based on the combined disclosures of Zoghbi et al., Falck-Pedersen et al., Bout et al., and Wigand et al. in the manner set forth by the Office.

2. *The Office Has Not Accorded Appropriate Weight to the Declarations Under 37 C.F.R. § 1.132 of Record*

The Rule 132 declarations of Douglas E. Brough filed on February 26, 2009, and December 17, 2009, demonstrate, *inter alia*, that certain non-subgroup C adenoviral vectors unexpectedly exhibit enhanced delivery to sensory cells of the inner ear as compared to a subgroup C adenoviral vector, and that this does not occur simply because the non-subgroup

C vector is not of subgroup C. In the Office Action dated March 24, 2010, the Office Action states that the results described in the Rule 132 declarations are "exactly as expected" in view of the prior art (Office Action at page 21, third complete paragraph), given that non-subgroup C adenoviral vectors were developed to overcome technical difficulties associated with subgroup C adenoviral vectors (i.e., Ad5). The Office also contends that the Rule 132 declarations are not persuasive because the claims are not directed to non-subgroup C adenoviral vectors which transduce inner ear cells more efficiently than subgroup C vectors (see Advisory Action dated July 20, 2010).

However, the evidence of superiority in a property that a claimed compound or method shares with the prior art can be used to rebut a *prima facie* case of obviousness. *In re Chupp*, 816 F.2d 643, 646, 2 U.S.P.Q.2d 1437, 1439 (Fed. Cir. 1987). While the claims do not recite that an Ad28 vector transduces supporting cells of the inner ear more efficiently than subgroup C adenoviral vectors, transduction of such cells is a necessary property of the claimed method. Indeed, expression of the nucleic acid sequence encoding Hath1 cannot occur unless inner ear cells are transduced by the Ad28 vector containing the Hath1 sequence. Therefore, the results described in the Rule 132 declarations are commensurate in scope with the appealed claims, and were not predictable from the cited references, whether considered alone or in the aggregate.

Furthermore, the Office has provided no evidence to support the allegation that non-subgroup C adenoviral vectors were developed solely to overcome technical difficulties associated with subgroup C adenoviral vectors. The technical difficulties referred to by the Office and referenced in the teachings of Falck-Pedersen relate to immune responses to Ad5 vectors. Whether a non-group C adenovector is more or less likely to trigger a host immune response is entirely irrelevant to the unexpected properties of enhanced delivery to sensory cells of the inner ear as described in the Rule 132 declarations.

For the foregoing reasons, the obviousness rejections are not well-founded. The Office has not properly considered the obviousness issue in accordance with established legal precedent – both with respect to considering whether there exists a credible reason for one of ordinary skill in the art to choose an Ad28 vector and with respect to properly considering the evidence of unexpected properties set forth in the Rule 132 declarations of record. Accordingly, the obviousness rejections should be withdrawn.